UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/342,993	06/29/1999	JUDES POIRIER	08523/005002	7392

21559 7590 04/13/2005

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/342,993	**Applicant(s)** POIRIER, JUDES	
	Examiner Karen Cochrane Carlson, Ph.D.	**Art Unit** 1653	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 18 February 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on *18 February 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-5,8 and 9*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 3. NOTE: Applicants have effectively shifted their invention back to the claims presented in an after-final amendment (12/23/2002), changing the claims to:

A method for the identification of human subjects having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the presence of apoE4 gene alleles in said subject, wherein the absence of an apoE4 gene allele in a biological sample of said subject identifies said subject as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

In the last advisory action prior to RCE, the Examiner stated that the invention had been shifted such that a new method was being claimed, that is, the apoE4 is an apoE allele (as are apoE2, apoE3, etc), and now Applicants are claiming choosing an allele within the apoE4 itself. For example, the claim now reads that, say 5 apoE4 alleles are found and that some of these are absent. This was/is considered to be a shift in the invention, and would require further search and consideration.

Note that on page 1, para 3 (and page 5, penultimate sentence) of the specification, the apoE gene has three common alleles (E2, E3, E4). The specification does not discuss alleles of apoE4; rather THE apoE4 is an allele of apoE and its absence is what determines responsiveness to cholinomimetic drugs. Thus, as claimed, there is an issue of new matter. Re: Applicants disccussion on page 9, the phrase "copies of the apoE4 gene allele" refers to the gene encoding the apoE4 allele, not that there would be different apoE4 alleles to choose from.

Applicants urge that the first action made final after RCE and after denial of the entry of claims presented in the previous after-final response was improper. The first office action on the merits mailed 8/4/2000 addressed :

A method for the identification of human subjects to be responsive to a cholinomimetic drug, said subjects having Alzheimer's disease, said method comprising determining the number of copies of apoE4 gene alleles in said subject, wherein the absence of apoE4 gene allele in a biological sample of said subject indicates a predisposition to respond to a cholinommimetic drug.

A CPA was filed by Applicants, and a Final (4/13/2001) and non-final (10/31/2001) rejections followed.

On 5/9/2002, Applicants amended their claims to eliminated "number of copies of apoE4 gene allele" to simply determining the presence of apoE4 alleles:

A method for the identification of human subjects to be responsive to a cholinomimetic drug, said subjects having Alzheimer's disease, said method comprising determining the presence of apoE4 gene alleles in said subject wherein the absence of apoE4 gene allele in a biological sample of said subject indicates a predisposition to receive beneficial effects from a cholinomimetic drug.

A final rejection and the filing of an after-final amendment (12/23/2002) followed, changing the claims to:

A method for the identification of human subjects having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the presence of apoE4 gene alleles in said subject, wherein the absence of an apoE4 gene allele in a biological sample of said subject identifies said subject as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

In the advisory action, the Examiner stated that the invention had been shifted such that a new method was being claimed, that is, the apoE4 is an apoE allele (as are apoE2, apoE3, etc), and now Applicants are claiming choosing an allele within the apoE4 itself. For example, the claim now reads that, say 5 apoE4 alleles are found and that some of these are absent. This was/is considered to be a shift in the invention, and would require further search and consideration.

An RCE was filed 6/18/2003, requesting entry of the claims that the Examiner already stated was a shift in the invention. An RCE is does not entitle Applicants to shift inventions, but rather to continue the examination of the elected invention.

A Notice of Non-Compliant amendment was mailed to Applicants on 10/7/2003, and re-iterated that a shift in invention is not permissible.

In response, the invention was shifted again (6/28/2004):

A method for the identification of .q human subject having Alzheimer's disease responsive to treatment with a cholinomimetic drug, said method comprising determining the apoE allele load of said subject,wherein the absence of an apoE4 gene allele in a biological sample of said subject identifies said subject as a subject whose Alzheimer's disease-related cognitive impairment is responsive to treatment with a cholinomimetic drug.

Instead of sending out another NON-BONAFIDE Notice of Non-Compliant Amendment that could possibly result in abandonment of the application, the Examiner chose to act on the amendments because the claims at least indicated that the absence of apoE4 allele (from the apoE alleles) would indicate a subject responsive to treatment of Alzheimer's with cholinomimetic drugs, as orginally claimed 5 years ago.

Therefore, the resulting FINAL REJECTION mailed 8/16/2004 was PROPER after RCE because the amended claims examined were not those denied entry in the after-final amendment dated 12/23/2002.

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER